

CLAIMS

What is claimed is:

- 5 1. A method of identifying individuals predisposed to alcohol tolerance and dependence comprising:
 - a) providing a sample from a human subject; and
 - b) screening said sample for a biomarker selected from the group consisting of Grid2, Efnb3, Grin1, Zfp179, Tceb11, Gria1, Sec8, Prdx5, Rad50,
10 Catna2, and B2m, wherein said biomarker is correlated with a predisposition to alcohol tolerance and dependence.
2. The method of Claim 1, wherein said biomarker is selected from the group consisting of Grid2, Efnb3, Grin1, Zfp179, Tceb11, Gria1, and Sec8, and wherein said biomarker
15 is associated with transcriptional upregulation.
3. The method of Claim 1, wherein said biomarker is selected from the group consisting of Prdx5, Rad50, Catna2, and B2m, and wherein said biomarker is associated with transcriptional downregulation.
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4. The method of Claim 1, wherein said screening is accomplished by quantitating the mRNA or protein level of said biomarker.
5. The method of Claim 4, wherein said mRNA level is quantitated by a method
25 selected from the group consisting of real time polymerase chain reaction, and gene expression array.
6. The method of Claim 1, wherein said screening is accomplished by detection of a polymorphism in said biomarker.

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7. The method of Claim 6, wherein said detection is accomplished using at least one technique selected from the group consisting of polymerase chain reaction, heteroduplex analysis, single stand conformational polymorphism analysis, ligase chain reaction, comparative
5 genome hybridisation, Southern blotting and sequencing.

8. A method of identifying individuals at reduced risk of developing alcohol dependence, comprising:

- a) providing a sample from a human subject; and
- 10 b) screening said sample for at least one biomarker of the 16p13.3 locus or the 16q12.2 locus, wherein said biomarker is correlated with a reduced risk of developing at least one symptom of alcohol dependence and/or with reduced alcohol consumption.

15 9. The method of Claim 8, wherein said biomarker is selected from the group consisting of the AC9 gene, the AC7 gene, and markers in linkage disequilibrium thereof, and wherein said screening is accomplished by detection of a polymorphism in said biomarker.

10 10. The method of Claim 9, wherein said biomarker is the AC9 gene, and said polymorphism is a [TAA]₉ repeat in an intron of said AC9 gene.

11. The method of Claim 9, wherein said biomarker is the AC7 gene, and said polymorphism is an [AACA]₇ repeat in the 3'-untranslated region of said AC7 gene.

25 12. The method of Claim 8, wherein said at least one symptom comprises a symptom selected from the group consisting of alcohol tolerance, alcohol withdrawal, heavy alcohol consumption, persistent desire to reduce alcohol consumption, considerable time spent in acquiring, using or recovering from alcohol, alcohol-related reduction in social, occupational, or recreational activities, and continued alcohol use despite alcohol-related physical or
30 psychological problems.

13. The method of Claim 9, wherein said detection is accomplished using at least one technique selected from the group consisting of polymerase chain reaction, heteroduplex analysis, single stand conformational polymorphism analysis, ligase chain reaction, comparative genome hybridisation, Southern blotting and sequencing.

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14. A method of identifying individuals at increased risk for alcohol abuse, comprising:

- a) providing a sample from a human subject; and
- b) screening said sample for at least one biomarker of the 16q12.2 locus, wherein said biomarker is correlated with increased risk of developing at least one symptom of alcohol abuse.

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15. The method of Claim 14, wherein said biomarker is selected from the group consisting of the AC7 gene and a marker in linkage disequilibrium with the AC7 gene, and wherein said screening is accomplished by detection of a polymorphism in said marker.

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16. The method of Claim 15, wherein said biomarker is the AC7 gene, and said polymorphism is an [AACA]₅ repeat in the 3'-untranslated region of said AC7 gene.

17. The method of Claim 14, wherein said at least one symptom comprises a symptom selected from the group consisting of recurrent alcohol use resulting in failure to fulfill major obligations, recurrent alcohol use in physically hazardous situations, recurrent alcohol-related legal problems, and continued alcohol use despite alcohol-related social problems.

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18. The method of Claim 15, wherein said detection is accomplished using at least one technique selected from the group consisting of polymerase chain reaction, heteroduplex analysis, single stand conformational polymorphism analysis, ligase chain reaction, comparative genome hybridisation, Southern blotting and sequencing.

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19. A kit for determining whether a subject is at a reduced or increased risk for developing alcohol abuse and/or dependence, comprising:

- a) at least one reagent capable of specifically detecting at least one polymorphism in an allele of a gene selected from the group consisting of AC9, AC7, and genes in linkage disequilibrium thereof; and
- b) instructions for determining whether a subject is at a reduced or increased risk of developing abuse and/or alcohol dependence.

20. The kit of Claim 19, wherein said at least one polymorphism is a microsatellite repeat polymorphism.

21. The kit of Claim 19, wherein said at least one reagent comprises a nucleic acid probe that hybridizes under stringent conditions to a nucleic acid sequence selected from the group consisting of the coding strand of said gene, and the noncoding strand of said gene.

22. The kit of Claim 19, wherein said at least one reagent comprises a sense primer and an antisense primer flanking said at least one polymorphism in said allele.

23. The kit of Claim 22, wherein at least one of said primers comprises a fluorescent tag.

24. A method of screening compounds, comprising:

- a) providing:
 - i) at least one allele of a gene selected from the group consisting of Grid2, Efnb3, Grin1, Zfp179, Tceb11, Gria1, Sec8, Prdx5, Rad50, Catna2, B2m, AC9, and AC7, or a cell transfected with said at least one allele of said gene, and
 - ii) one or more test compounds; and
- b) contacting said gene or said cell with said test compound; and
- c) detecting a change in expression of said gene in the presence of said test compound relative to the absence of said test compound.

25. The method of Claim 24, wherein said detecting comprises detecting RNA transcribed from said gene.

5 26. The method of Claim 24, wherein said detecting comprises detecting a polypeptide encoded by said gene.

27. The method of Claim 24, wherein said gene is contained within an eukaryotic cell when contacting said gene with said test compound.

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28. The method of Claim 24, wherein said gene is contained within an *in vitro* transcription reaction when contacting said gene with said test compound.